



Docket No. 50046290-0007 (UTN-106099)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Imre U.S. Patent Application of
Naidu, Satyanarayan A.

Serial No.: 09/980,062

Filed: May 26, 2000

For: IMMOBILIZED LACTOFERRIN
(Im-LF) ANTIMICROBIAL AGENTS AND
USES THEREOF

Examiner: Russel, Jeffrey E.
Group Art Unit 1654

SUPPLEMENTAL RESPONSE TO
OFFICE ACTION DATED JANUARY 12, 2004

Mail Stop – NON-FEE AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In conjunction with the Amendment mailed by Applicant's attorney on July 12, 2004, please consider the attached Declaration of Dr. Andrew R. Barron (see *Exhibit A*).

As explained by Dr. Barron, lactoferrin (LF) has a bilboate structure, with a positively charged N-terminus lobe and a negatively charged C-terminus lobe. (Barron Decl., Par. 7.) A full length LF peptide sequence has about 600 to about 800 continuous amino acids. (*Id.*) Human LF, in particular, is about 703 amino acids long and has a molecular weight of about 83,000 daltons. (*Id.*)

The instant application describes LF immobilized on a naturally occurring substrate via its N-terminus region, *i.e.*, LF having its N-terminus region attached to a substrate leaving the C-terminus region free. (Appl. page 7, line 34-page 8, line 3.) For LF to become immobilized on a substrate and, in particular on a naturally occurring substrate, the portion of the substrate which is to do the binding should carry the opposite charge, *i.e.*, carry a positive charge. (Barron Decl., Par. 8.)

The Examiner rejected claims 102-104, 115-117, 119, 124, 127, 128, 137, 138, 142-148, 154, 157, 158, 171, 172, 176, 179, 180, 186, and 193-196 under 35 U.S.C. 102(e). Gohlke *et al.* describe compositions containing a combination of colostrum and lactoferrin in a "mucosal delivery format" ("MDF"). (Col. 6, lines 13-28.) The composition can also contain modified pectin. (Col. 6, lines 49-52.) By MDF is meant a composition, such as a lozenge, formed of solid components. (Barron Decl., Par. 11.) For example, Gohlke *et al.* teach, "The individual components of the composition may be obtained from commercial sources: colostrum (which is dehydrated by standard spray-drying procedures known in the art)" (col. 9, lines 41-44). Furthermore, examples 1 - 3 describe a process for preparing the compositions where, "[E]ach of the following ingredients is placed, in powdered form, into a commercial mixer." The ingredients are then mixed and cold pressed.

The mere presence of LF in a cold-pressed mixture with dehydrated colostrum or modified pectin would not result in the immobilization of the LF via its N-terminus. (Barron Decl., Par. 13.) Moreover, Gohlke *et al.* do not disclose nor suggest any conditions under which the compounds could be mixed to result in the LF becoming attached via its N-terminus. (Barron Decl., Par. 14.) For example, mixing LF with colostrum (and modified pectin) and cold pressing will not provide an environment suitable to cause the LF to become attached to colostrum or to modified pectin via LF's N-terminus region. (*Id.*)

The examiner rejected claims 1, 2, 11, 18, 19, 28, 31, 39, 101-103, 119-124, 126-129, 131, 132, 134, 142-151, 153, 164, 171-173, 175, 186, 193-195, 197, and 200 under 35 USC §102(b) as being anticipated by or under 35 USC §103(a) as obvious in view of WO Patent Application 91/13982 ("WO Patent Application '982"). WO Patent Application '982 generally relates to human LF expressed using recombinant DNA. It discloses the use of this LF as a nutritional supplement, an antiseptic, and as a food-spoilage retardant. The LF can be compounded with certain carriers or diluents.

However, WO Patent Application '982 neither broadly teaches LF immobilized on a naturally occurring substrate via the N-terminus region of the LF, nor does it provide a specific example of such an immobilized LF. (Barron Decl., Par. 15.) The examiner asserts that:

"The WO Patent Application '982 teaches LF in combination with stearic acid (which is a lipid and also corresponds to Applicant's pharmaceutically acceptable carrier of claim 102) or its salts . . . Because the same components are present in the same defined dispersion, inherently the LF in the composition of the WO Patent Application '982 will be immobilized via its N-terminus . . ."

But, stearic acid with a molecular weight of only 284.47 is not a substrate on which LF can be immobilized. (Barron Decl., Par. 17.) Furthermore, WO Patent Application '982 does not disclose nor suggest any other carriers or diluents that would be reactive with the N-terminus of LF and immobilize LF. (Barron Decl., Par. 18.)

The mere presence in a mixture of LF and stearic acid or any of the other naturally occurring carriers or diluents taught in WO Patent Application '982 would not inherently result in immobilization of the LF via its N-terminus on a substrate. (Barron Decl., Par. 19.) The reference does not disclose or suggest any conditions under which the compounds could be mixed to achieve such immobilization. (Barron Decl., Par. 20.) Merely compounding solid LF with a solid stearic acid carrier, such as by cold-pressing the solid ingredients, will not provide an environment suitable to cause the LF to become immobilized via its N-terminus region. (*Id.*)

The examiner rejected claims 1, 2, 5, 18, 19, 22, 31, 38, 39, 101-103, 106, 115-117, 119-124, 126-129, 131-132, 134, 136, 142-151, 153, 164, 171-173, 175, 186, 193-197, and 200-202 under 35 USC § 102(b) as being anticipated by or under 35 USC § 103(a) as obvious in view of European Patent Application 753,309 (European Patent Application '309). European Patent Application '309 generally relates to the preparation of mixtures of lactoferrin and desferrioxamine methanesulphonate useful for the therapy of viral infectious diseases.

However, European Patent Application '309 neither broadly teaches LF immobilized on a naturally occurring substrate via the N-terminus region of the LF, nor does it provide a specific example of such an immobilized LF. (Barron Decl., Par. 21.) The examiner asserts that:

"The European Patent Application '309 teaches compositions comprising LF and carriers such as paraffin oil and Vaseline (which are lipids), xantan gum and corn starch (which are polysaccharides), and lecithin (which is an emulsifier) Because the same components are

present in the same defined dispersion, inherently the LF
in the composition of the European Patent Application
'309 will be immobilized by its N-terminus . . . "

But, paraffin oil and Vaseline are low molecular weight compounds, not substrates. (Barron Decl., Par. 23.) LF could not become immobilized on such small molecules. (*Id.*) Additionally, paraffin oil and Vaseline are hydrocarbons (not lipids) and do not carry any charge. (Barron Decl., Par 25.) As a result, neither paraffin oil nor Vaseline contains a region, which will attach LF's positively charged N-terminus region. (*Id.*)

Further, xanthan gum and cornstarch do not carry any charges. (Barron Decl., Par. 26.) As a result, neither xanthan gum nor cornstarch contains a region, which will attach LF's positively charged N-terminus region. (*Id.*) Still further, lecithin is a low molecular weight compound. (Barron Decl., Par. 27.) LF could not become immobilized on such a small molecule. (*Id.*)

The examiner rejected claims 1, 2, 5, 18, 19, 22, 31, 32, 38, 39, 101-103, 106, 115, 119-124, 126-129, 131-136, 142-151, 153, 162-165, 171-173, 181, 184-187, 193-197, and 200-202 under 35 USC §102(b) as being anticipated by or under 35 USC §103(a) as obvious in view of European Patent Application 753,308 (European Patent Application '308). European Patent Application '308 generally relates to the use of LF for therapy of diseases caused by Gram-positive pathogen microorganisms. However, European Patent Application '308 neither broadly teaches LF immobilized on a naturally occurring substrate via the N-terminus region of the LF, nor does it provide a specific example of such an immobilized LF. (Barron Decl., Par. 28.) The examiner asserts that:

"The European Patent Application '308 teaches compositions comprising LF and peppermint oil, gum base and corn starch (which are polysaccharides) . . . Because the same components are present in the same defined dispersion, inherently the LF in the composition of the European Patent Application '308 will be immobilized via its N-terminus . . . "

But, peppermint oil is a low molecular weight compound. (Barron Decl., Par. 30.) LF could not become immobilized on such a small molecule. (*Id.*)

Furthermore, peppermint oil, gum base, and cornstarch do not carry any charges. (Barron Decl., Par. 31.) As a result, neither peppermint oil, gum base nor cornstarch contains a region, which will attach LF's positively charged N-terminus region. (*Id.*)

The examiner rejected claims 1-3, 5, 18-20, 22, 31, 32, 102-104, 106, 115, 119, 124, 137, 138, 142-150, 154, 164, and 165 under 35 USC § 102(e) as being anticipated by US Patent 6,066,469 by Kruzel *et al.* ("Kruzel *et al.*"). This patent discloses the use of LF as a nutritional supplement, an antiseptic, to treat and prevent opportunistic bacterial, viral and fungal infections, and as a food-spoilage retardant. It neither broadly teaches LF immobilized on a naturally occurring substrate via the N-terminus region of the LF, nor does it provide a specific example of such an immobilized LF. (Barron Decl., Par. 32.) The examiner asserts that:

"Kruzel *et al.* teach nutritional supplements comprising LF in combination with adjuvants or diluents such as cellulose, starch, tragacanth, and sodium carboxymethylcellulose . . . Because the same

components are present in the same defined dispersion,
inherently the LF in the nutritional supplements of
Kruzel et al will be immobilized via its N-terminus . . . "

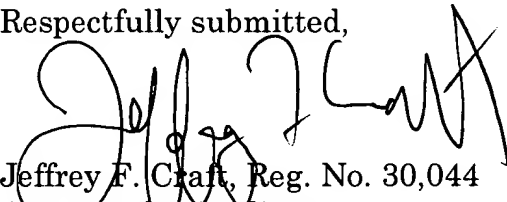
But, the mere presence in a mixture of LF and any of the adjuvants or diluents, such the solids cellulose, starch, tragacanth, or sodium carboxymethylcellulose would *not* inherently result in immobilization of the LF via its N-terminus. (Barron Decl., Par. 34.) Kruzel *et al.* does not disclose nor suggest any conditions under which the compounds could be mixed to result in the LF becoming attached via its N-terminus. (Barron Decl., Par. 35.)

Furthermore, cellulose and starch do not carry any charges. (Barron Decl., Par. 36.) As a result, neither cellulose nor starch contains a region, which will attach to LF's positively charged N-terminus. (Barron Decl., Par. 37.)

CONCLUSION

In light of the amendments and remarks presented in the Amendment mailed July 12, 2004 and the Declaration of Dr. Barron, it is believed that the application is in condition for allowance, so that a prompt and favorable action is respectfully requested.

Respectfully submitted,



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